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A Case of Colonoscopy-induced Wunderlich's syndrome in a hemodialysis patient: Coincidence or Link?

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Abstract

Wunderlich syndrome is a rare condition encountered in patients undergoing chronic hemodialysis (HD) usually attributed to acquired cystic kidney disease (ACKD) among other causes. However, presentation of renal hemorrhage after colonoscopy, to the best of our knowledge, has not been previously documented. Nevertheless, only splenic injury was rarely mentioned. Management can range from conservative treatment to angiographic embolization or exploration and nephrectomy. We report an unusual case of a 54-year-old woman HD patient who presented with SRH within a few days of colonoscopy. The reason of spontaneous renal hemorrhage (SRH) was rupture of a cyst of ACKD. We assumed that colonoscopy was a provoking factor and elaborated hypotheses for its etiopathogenesis. The patient underwent left successful nephrectomy. The importance of this case lies in the fact that colonoscopy is not always an innocent procedure in HD patients, and could be complicated by renal cyst hemorrhage.

Keywords: Spontaneous renal hemorrhage, Hemodialysis, Acquired cystic renal disease, Colonoscopy.

Introduction

Wunderlich syndrome, also known as SRH is a rare and potentially fatal condition in patients undergoing hemodialysis (HD) that is attributed to acquired cystic kidney disease (ACKD) among other plentiful causes most commonly being angiomyolipoma and renal cell carcinoma (RCC) while vascular entities such as polyarteritis nodosa and Wegener polyangiitis being rare.<sup>1</sup> Most published cases following colonoscopy discuss splenic rupture as unusual complication, and may present in 1-21/100000 of cases.<sup>2</sup> To the best of our knowledge SRH has never been described before as a complication of renal cyst rupture in ACKD after colonoscopy. We describe a HD patient with ACKD who developed SRH after colonoscopy along with a discussion of the contributing factors and highlight that HD patients should be under close surveillance after gastrointestinal endoscopy. We report this case because of its rarity and significance with respect to being a complication in a dialysis patient.

Case presentation

A 54-year-old Lebanese woman, on maintenance hemodialysis (HD) twice weekly for focal segmental glomerulosclerosis (FSGS) was admitted to the emergency department, after she had undergone her scheduled hemodialysis the day before, for sudden onset of severe left flank pain, nausea, and vomiting. The pain had started suddenly about 12 hours prior to presentation and worsened rapidly. On a side note, a severe secondary hyperparathyroidism with cutaneous calciphylaxis was treated by cinacalcet for 3 years without response required parathyroidectomy (four glands hyperplasia) 8 months before her current admission. Five days prior to presentation, she was admitted to the hospital because of severe anemia and rectorrhagia. Her renal ultrasound evaluation showed bilaterally small kidneys with thinned parenchyma containing cysts up to 3 cm and vascular calcifications without hydronephrosis. Colonoscopy through terminal ileum revealed a 7 mm polyp in the left descending colon which was removed by mucosectomy. Microscopy returned as sessile tubular adenoma with low-grade dysplasia. The patient denied fever or a history of trauma. There was no previous history of antiplatelet use. In the emergency department, her blood pressure and pulse rate were 112/65mmHg and 96 bpm, her temperature was 36.8<sup>[2]</sup>C and she had mildly distended abdomen with severe left costovertebral angle tenderness. Laboratory findings showed Hemoglobin 9.0 gm/dL while hematocrit was 29.7%, total leucocyte count 12.2 × 1000/microliter creatinine: 6.06mg/dL); C-Reactive Protein level: 6 mg/L.. In addition, PT was 83% and INR was 1.13. A multiphasic computed tomography (CT) scan of the thorax, abdomen and pelvis was performed without and with intravenous contrast. The scan revealed a large cyst and huge distorting left perirenal intraparenchymal hematomas with a subcapsular collection up to 1.8 cm thick with hematic collection throughout the renal compartment reaching a diameter of more than 9x4 cm, left hydronephrosis and edema surrounding fat throughout the flank and calcifications in the hilum (Figure 1). For decompression of the renal pelvicalyceal system and drainage, we chose to treat her with retrograde left double-J ureteral stent insertion which identified a clot in the left mid-ureter and urine culture and cytology were taken and were negative. Plain film of abdomen showed the double J in place (Figure 2). The patient remained hemodynamically stable but with further drop in hemoglobin (6.1 g/dL) the same evening, mandates a transfusion of one unit of leuco-depleted red cell concentrate for stabilization. A decision was made for surgical exploration with presumptive diagnosis of subacute left perirenal hematoma and for exclusion of underlying malignancy. She underwent a HD session without heparin. On day 3, she underwent open radical left nephrectomy with conservation of the adrenal gland. She received 2 more units of leuco-depleted red cell concentrate packed during the intervention. The renal parenchyma is almost entirely replaced by a hematoma measuring 9x9x7 cm and extending into the peri-renal fat. A small papillary mass was sent separately. The detailed histopathological evaluation revealed a renal parenchyma with lesions of chronic nephritis mutilated by large hemorrhagic areas which extend to the peri-renal fat. In addition, there was a neoplastic proliferation, measuring 2 mm, with papillary architecture covered by little atypical cubic cells and foamy macrophages in the axis compatible with papillary adenoma. On next operative day the patient underwent HD and received a pack of leuco-depleted red blood cells. The post-operative period was uneventful. Hemoglobin level remained around 10 g/dL. She was discharged on the seventh day without any bleeding sign or symptoms. She remains well and asymptomatic and is meanwhile on regular maintenance HD.

## Discussion

Since it was first described in 1856, spontaneous renal hemorrhage (SRH) has been reported infrequently in the literature, where dialysis patients are often excluded. Classic symptoms, such as acute flank pain, flank mass, and signs of internal bleeding, known as Lenk's triad, have limited sensitivity and specificity for detecting SRH.<sup>3</sup> Nowadays, computed tomography (CT) is the method of choice for the diagnosis. Most frequent etiologies are renal cysts, benign and malignant renal tumors, vascular lesions, and antiplatelet or anticoagulant therapy.<sup>3</sup>

ACKD is a well-known late stage complication of end-stage renal disease (ESRD). It can develop in up to 74% of patients with end-stage renal failure undergoing chronic HD lasting more than four years.<sup>3</sup> The prevalence of ACKD is directly related to the duration of dialysis and cysts tend to grow with time. Numerous complications have been described in relation to this entity including lithiasis, infection, urinary tract obstruction, malignant degeneration and intracystic bleeding that can cause a spontaneous retroperitoneal

hemorrhage (RH). Hemorrhagic renal cysts are the most frequent complication of patients with ACKD.<sup>4</sup> Bleeding is usually confined within the cyst but occasionally extends into the renal collecting system leading to hematuria or into the perinephric space leading to perirenal hematoma, or RH. Perinephric hematomas have been reported in up to 13% of patients with ACKD.<sup>3</sup> Among dialysis patients, ACKD has been recognized to be the most frequent cause. Approximately 50% of patients with ACKD develop hemorrhagic renal cysts.<sup>4</sup> Malek-Marín et al. reported a single center incidence of SRH in hemodialysis patients as 0.86 cases/100 patients.<sup>5</sup> When SRH was of renal origin in dialysis patients, the most common cause was cyst rupture in patients with ACKD.<sup>5</sup> The usual definition of ACKD requires three or more cysts per kidney in a patient on dialysis who does not have a hereditary cause of cystic disease. Within the first 3 years of dialysis, approximately 10–20% of patients develop ACKD. By 5 years, 40–60% of patients have ACKD and by 10 years more than 90% of patients exhibit ACKD.<sup>6</sup> Our patient had risk factors for development of ACKD, including long duration of renal replacement therapy. Moreover, our patient did not have any cysts in the kidney at the start of the dialysis. Nephrectomy material also histologically confirmed the diagnosis of ACKD. It is well documented that pre-existing renal disease can predispose a kidney to injury. Another notable observation in SRH secondary to cyst rupture is that there is a remarkable difference in frequencies between SRH due to ACKD and Autosomal dominant polycystic kidney disease (ADPKD). Most of the described patients in the literature had underlying ACKD rather than ADPKD. Some putative factors have been put forward to explain this disparity. The more medullary location of cysts in ADPKD compared with cortically residing cysts of ACKD and differences in the speed of cyst growth might account for differences in observed prevalence of SRH.<sup>5</sup> Among hemodialysis patients, perirenal or retroperitoneal bleeding due to acquired cyst rupture tends to occur after the dialysis session, possibly as a consequence of heparinization.<sup>6</sup>

Although the mechanism of SRH in the present case remains elusive; several factors might have contributed to the bleeding. First, the histories of hyperparathyroidism, uremia, chronic HD, and atrophied kidney with cystic change of ACKD were risks for hemorrhage. Second, the patient received her heparin dose the day before the colonoscopy. Third, the presence of calciphylaxis, also known as calcific uremic arteriolopathy, should also be considered. It has been reported in 1% to 4.5% of patients in dialysis with vascular calcifications with calcium oxalate crystals tissues depositions.<sup>7</sup> Our patient had diffused small artery calcification and calcium oxalate crystals in her left nephrectomy specimen and her skin lesions of calciphylaxis where healed progressively after parathyroidectomy. Fourth, it would be difficult to establish that maneuvers performed during colonoscopy and endoscopic mucosal resection (EMR) as the cause of SRH due to the anatomical proximity the left kidney which is posterior to the descending colon, we believe that elevated intraluminal pressure as well as increased intraperitoneal pressure from gas insufflation during and external pressure on the left hypochondrium exacerbated by ileus from deep sedation, since patients cannot report pain associated with stretching, that also may contribute to increased perinephric pressure. Finally, it should be pointed out that renal cysts of ACKD are associated with fragile vessels focally calcified stretched across their distended walls, as in our patient, with thickened hypertrophic intima and fibrosis. When intracystic pressure rises, these vessels may leak blood into the cyst, causing it to expand rapidly, resulting in severe pain. If bleeding continues, then the cyst may rupture into the collecting system or, alternatively, it may rupture into the subcapsular compartment and eventually dissect through the renal capsule to fill the retroperitoneal space.

Since most of the clinically overt SRH cases in dialysis patients are secondary to rupture of acquired cysts, especially after 5 years of renal replacement therapy, patients should be screened for the presence of ACKD; this surveillance should be continued because of risk of cyst enlargement and malignancy. Because of the high probability of small clinical non-apparent underlying malignancy in HD patients who had ACKD with SRH, nephrectomy was necessary in our anuric patient.

## Conclusion

SRH is rare but important and potentially fatal complication. It is most probably underestimated in frequency in daily practice. We described a HD patient with ACKD who developed SRH after colonoscopy and we believe that this procedure has not been reported before as an underlying precipitating etiology. The reason of SRH was rupture of cysts of ACKD. HD patients should be under close surveillance related to ACKD

development and associated bleeding risks after colonoscopy. Finally, reporting of similar cases in medical literature seems necessary to shed more light on this obscure entity and increase the awareness among clinicians.

Conflict of Interest: No conflict of interest was declared by the authors.

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Figure 1: coronal CT scan section showing the left perirenal intraparenchymal hematoma with a subcapsular collection up to 1.8 cm thick

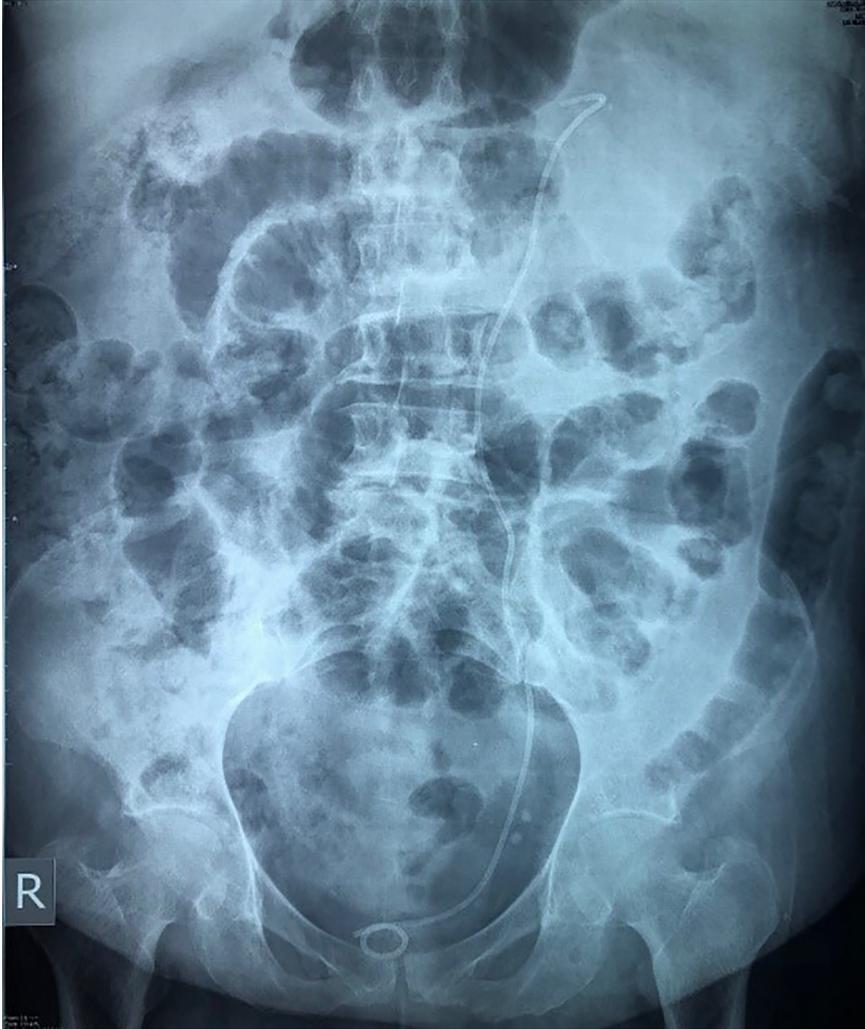


Figure 2: X-ray KUB showing the left JJ in place, as well as the diffuse colonic distention corresponding to ileus post colonoscopy